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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,301	07/27/2001	Roberto A. Macina	DEX-0188	8552
26259	7590	03/26/2004	EXAMINER	
LICATLA & TYRRELL P.C.			HOLLERAN, ANNE L	
66 E. MAIN STREET				
MARLTON, NJ 08053			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 03/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/806,301	Applicant(s) MACINA, ROBERTO A.	
	Examiner Anne Holleran	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 December 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>5/6/2002</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The amendment filed Dec. 22, 2003 is acknowledged. Claims 2-10 were canceled.
Claim 1 is pending and examined on the merits.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. References AQ, AZ - BL, BN - BS, BU, BV and BX – CB cited in the IDS filed May 6, 2002 have been considered. An initialed and signed PTO 1449 is included with the Office action.

Claim Rejections Withdrawn:

4. The rejection of claims 1-5 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the amendment.
5. The rejection of claim 1 under 35 U.S.C. 102(e) as being anticipated by Watson (U.S. Patent 6,566,072; issued May 20, 2003; filing date Sep. 29, 1998) is withdrawn in view of the amendment.
6. The rejection of claims 1 and 6 under 35 U.S.C. 102(e) as being anticipated by Billing-Medel (U.S. Patent 6,183,952; issued Feb. 6, 2001; filing date Aug. 15, 1997) is withdrawn in view of the amendment.

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Claim Rejections Maintained:

7. The rejection of claim 1 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for diagnosis of breast cancer, does not reasonably provide enablement for diagnosis of prostate cancer or any gynecologic cancer; or for the diagnosis of metastasis, for the monitoring of change in stage, or the monitoring of onset of metastasis of prostate cancer or any gynecologic cancer is maintained.

In view of the amendment changing the scope of the claims to exclude the detection of breast cancer, claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's amendment of claim 1 fails to overcome the grounds of rejection. As amended, claim 1 is drawn to methods for detecting prostate, ovarian or uterine cancer comprising measuring levels of ESBPII polypeptide encoded by SEQ ID NO: 1 or comprising SEQ ID NO: 2 in cells, tissues or bodily fluids in a patient; and comparing the measured levels of ESBPII polypeptide with levels of ESBPII polypeptide in cells, tissues or bodily fluids from a normal human control, where a change in measured levels of ESBPII polypeptide in said patient versus normal human control is associated with the presence of prostate cancer, ovarian cancer or uterine cancer.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence

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or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The full scope of claim 1 is not enabled by the specification, because the specification fails to establish that measuring levels of a polypeptide having the sequence of SEQ ID NO: 2, or any other protein that is to be considered an ESBPII polypeptide, may be used for the detection of prostate cancer or any gynecologic cancer other than breast cancer. Claim 1 is not enabled by the specification to the extent that the claims read on using measurements of protein levels as a basis for a method for diagnosis, staging or monitoring a change in cancer stage, because the data consists of mRNA measurements without any parallel detection of protein. Even if the data of Table 2 could be used to establish that measurements of mRNA levels were diagnostic of prostate, ovarian or uterine cancer, it is not predictable that measurements of the encoded protein also could be used as a basis for such diagnostic tests. Many proteins are regulated at the translational level rather than the transcriptional level. For instance, Shantz and Pegg (*Int J of Biochem and Cell Biol.*, 1999, Vol. 31, pp. 107-122) teach that ornithine decarboxylase is highly regulated in the cell at the level of translation and that translation of ornithine decarboxylase mRNA is dependent on the secondary structure of the mRNA and the availability of eIF-4E, which mediates translation initiation. McClean and Hill (*Eur J of Cancer*, 1993, vol. 29A, pp.2243-2248) teach that p-glycoprotein can be over-expressed in CHO cells following exposure to radiation, without any concomitant over-expression of the p-glycoprotein mRNA. In addition, Fu et al (*EMBO Journal*, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients

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with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Thus, steady state levels of protein are not necessarily correlated to steady state levels of mRNA, because of the homeostatic factors affecting transcription and translation.

Applicant's arguments have been carefully considered, but are unpersuasive. As a preliminary matter, it is noted that applicant failed to address one of the grounds of the rejection. In the rejection, two points were made. One point was that the data in Tables 1 and 2 showed that some cancers exhibited increased mRNA levels, others decreased mRNA levels and some no change in mRNA levels. Thus, the specification failed to provide a correlation between over-expression or under-expression of the mRNA with the detection of cancer. The second point was that the specification failed to demonstrate parallel protein measurements, and that demonstration mRNA differential expression was not necessarily evidence of differential protein expression. Applicant failed to address the second point. The argument that the data of Tables 1 and 2 is sufficient to enable the claimed methods because the data is similar to data provided for the diagnosis of breast cancer is not sufficient to obviate this rejection. The conclusion that the detection of ESBPII is useful for the detection of breast cancer was not made on the basis of the data provided in the specification, but on the basis of the teachings of the prior art.

Because the specification appears to be merely an invitation for further research to establish a correlation between levels of ESBPII protein levels and prostate, ovarian or uterine cancer, further undue experimentation would be required for the practice of the claimed inventions. Further, because there is no data in the specification demonstrating a correlation between protein levels and prostate, ovarian or uterine cancer, and because one cannot assume that a change in steady state levels of mRNA corresponds to a similar change in steady state

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levels of protein, the specification fails to establish that measurement of ESBPII protein levels could be used as the basis for the claimed method.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (571) 272-0833. Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D. can be reached at (571) 272-0871.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (571) 272-1600.

Anne L. Holleran
Patent Examiner
March 22, 2004


GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600